
Aryl hydrocarbon receptor antagonists promote the expansion of human hematopoietic stem cells.

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Public Summary:

Although practiced clinically for more than 40 years, the use of hematopoietic stem cell (HSC) transplants remains limited by the ability to expand these cells ex vivo. An unbiased screen with primary human HSCs identified a purine derivative, StemRegenin 1 (SR1), that promotes the ex vivo expansion of CD34⁺ cells. Culture of HSCs with SR1 led to a 50-fold increase in cells expressing CD34 and a 17-fold increase in cells that retain the ability to engraft immunodeficient mice. Mechanistic studies show that SR1 acts by antagonizing the aryl hydrocarbon receptor (AHR). The identification of SR1 and AHR modulation as a means to induce ex vivo HSC expansion should facilitate the clinical use of HSC therapy.

Scientific Abstract:

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